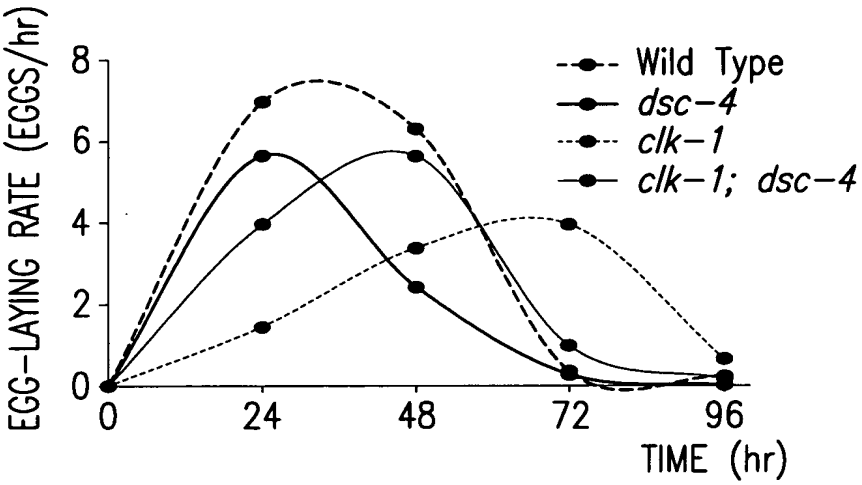

EGG-LAYING RATE (EGGS/hr)
8
6
4
2
0
0
24
48
72
96
TIME (hr)
Wild Type
dsc-4
clk-1
clk-1; dsc-4

FIG. 1A

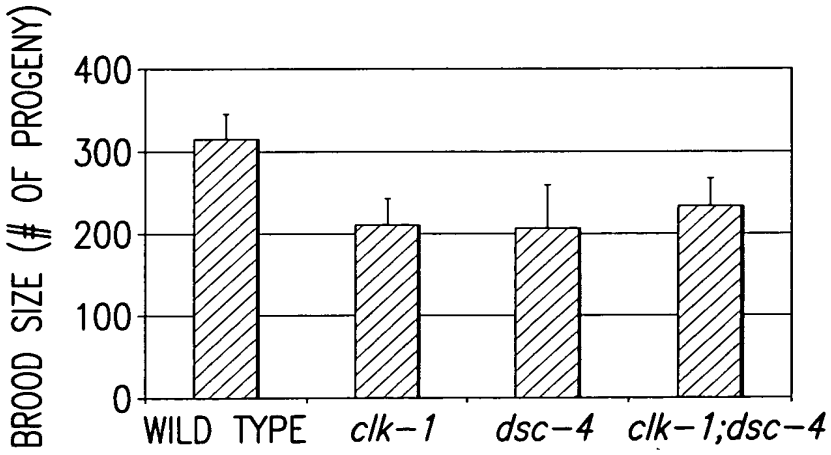

BROOD SIZE (# OF PROGENY)
400
300
200
100
0
WILD TYPE
clk-1
dsc-4
clk-1;dsc-4

FIG. 1B

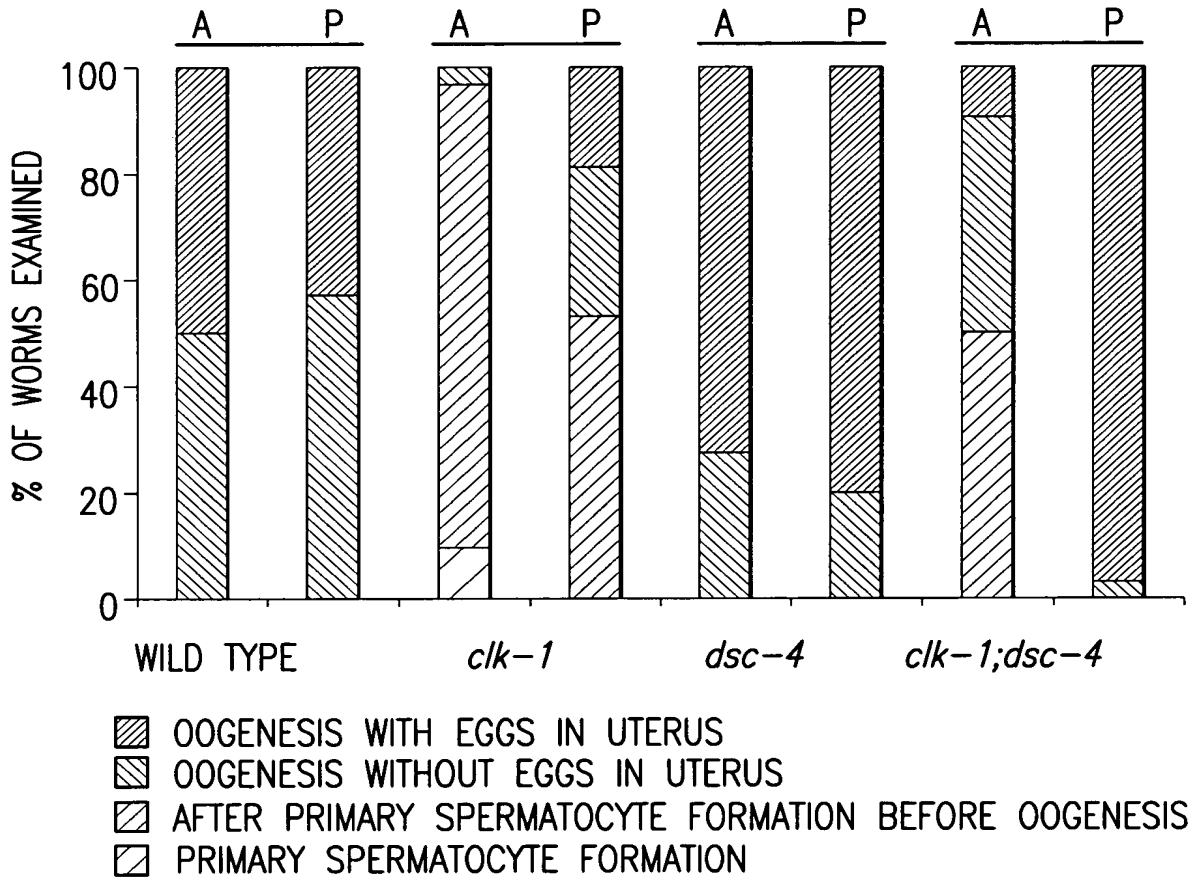

A
P
A
P
A
P
A
P
100
80
60
40
20
0
% OF WORMS EXAMINED
WILD TYPE
clk-1
dsc-4
clk-1;dsc-4
OOGENESIS WITH EGGS IN UTERUS
OOGENESIS WITHOUT EGGS IN UTERUS
AFTER PRIMARY SPERMATOCYTE FORMATION BEFORE OOGENESIS
PRIMARY SPERMATOCYTE FORMATION

FIG.1C

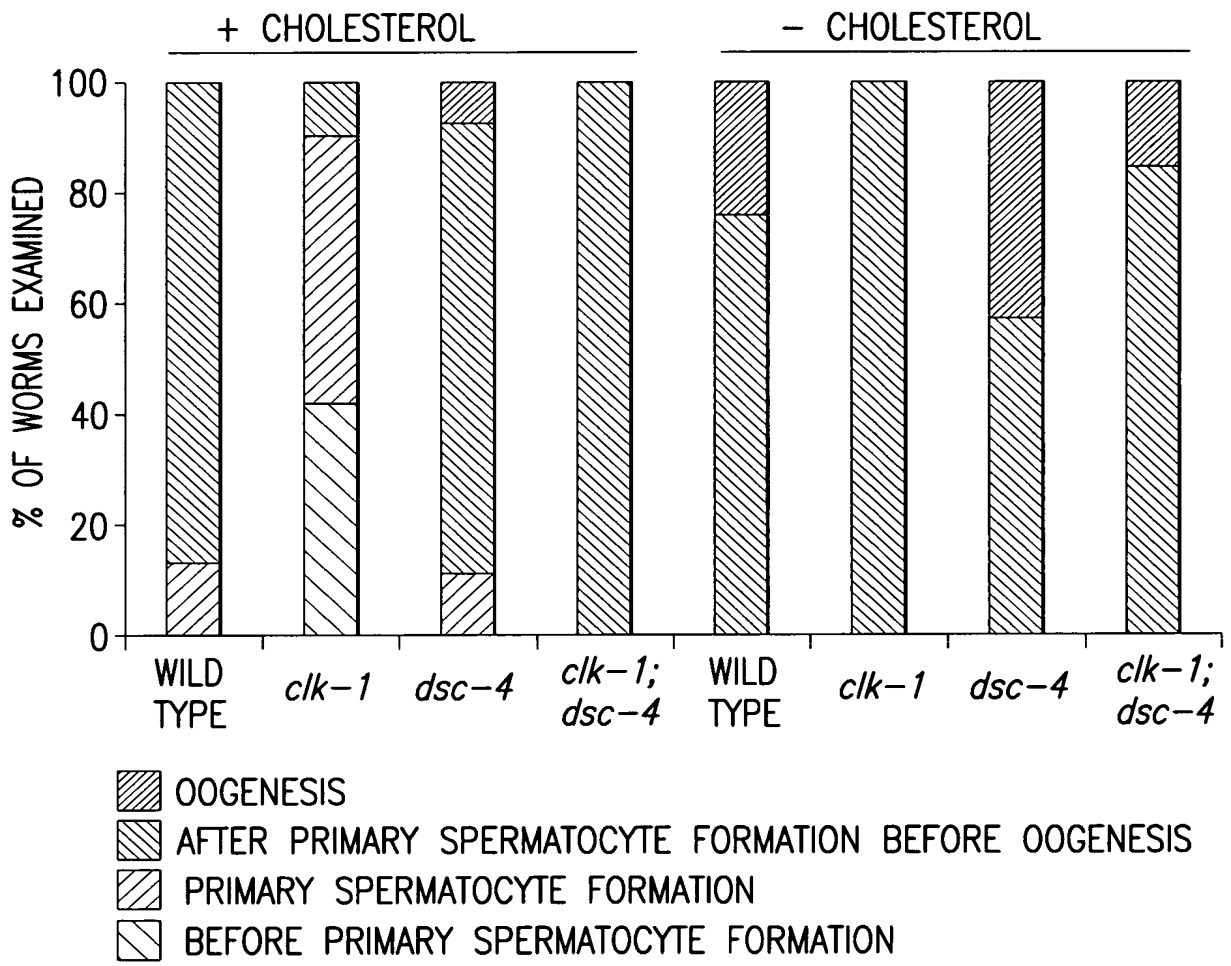

+ CHOLESTEROL
– CHOLESTEROL
% OF WORMS EXAMINED
100
80
60
40
20
0
WILD TYPE
clk–1
dsc–4
clk–1; dsc–4
WILD TYPE
clk–1
dsc–4
clk–1; dsc–4
OOGENESIS
AFTER PRIMARY SPERMATOCYTE FORMATION BEFORE OOGENESIS
PRIMARY SPERMATOCYTE FORMATION
BEFORE PRIMARY SPERMATOCYTE FORMATION

FIG. 1D

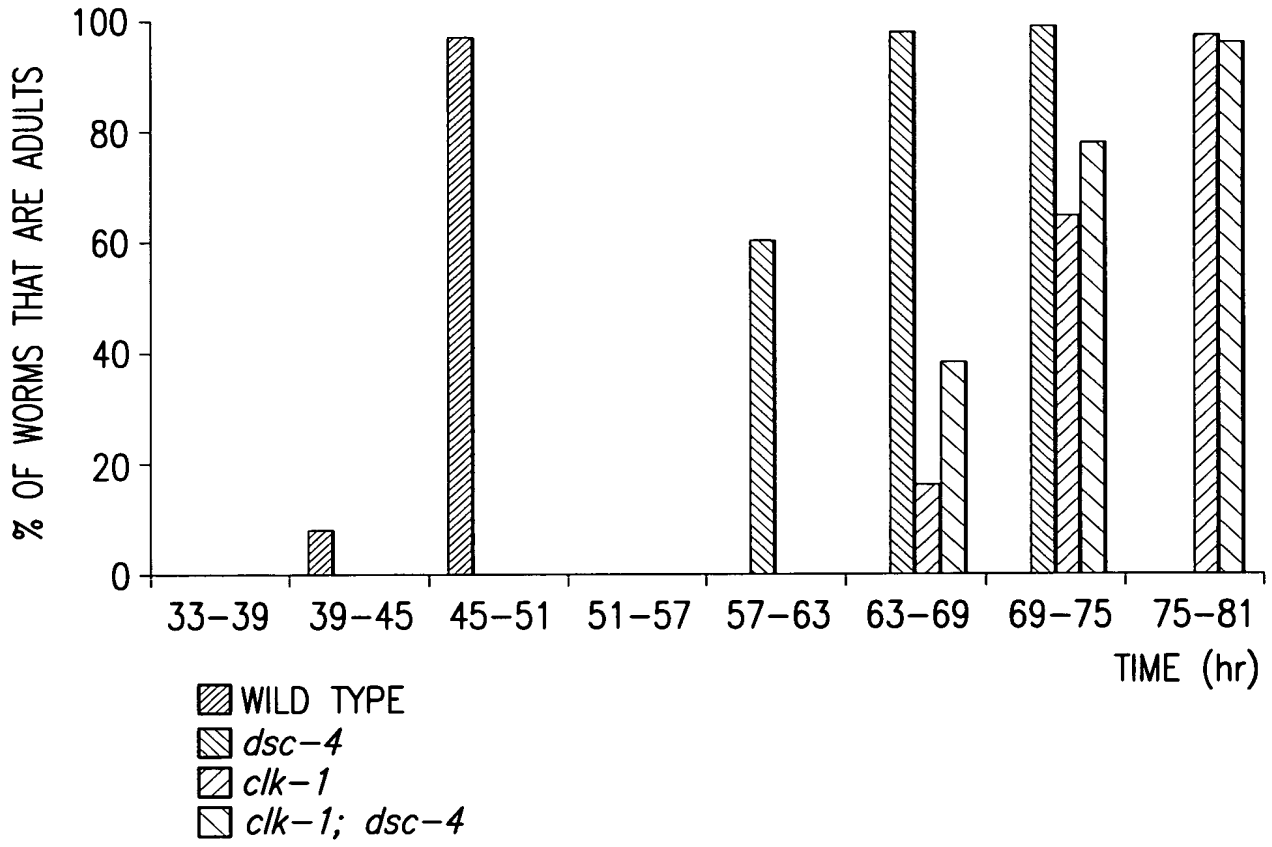

% OF WORMS THAT ARE ADULTS
100
80
60
40
20
0
33–39
39–45
45–51
51–57
57–63
63–69
69–75
75–81
TIME (hr)
WILD TYPE
dsc–4
clk–1
clk–1; dsc–4

FIG. 1E

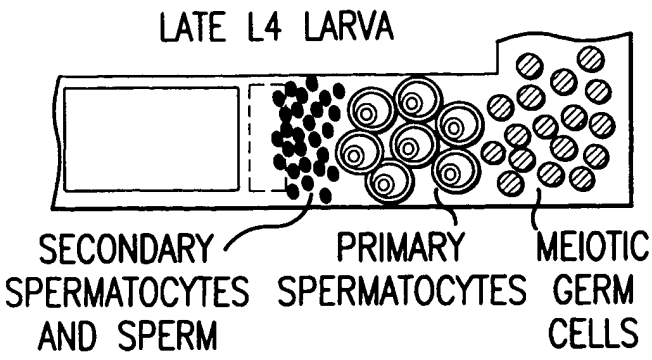


FIG.2A-1

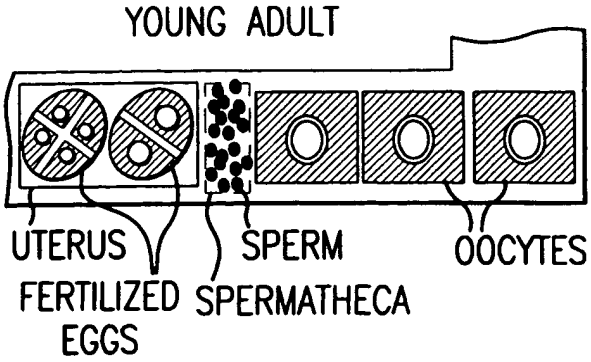


FIG.2A-2

FIG.2B

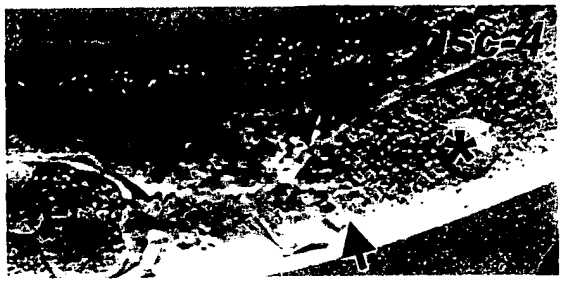
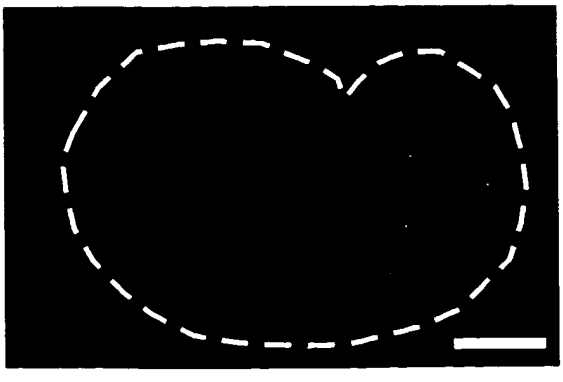
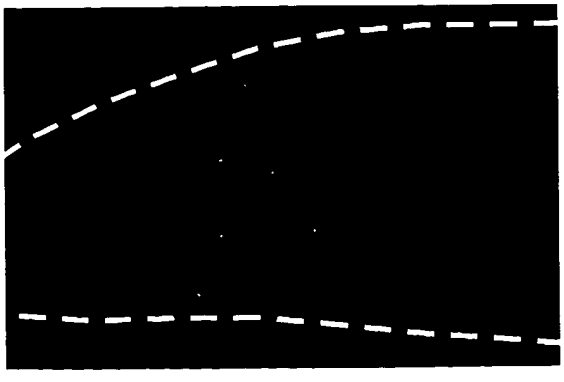


FIG.2C

FIG.2D

FIG.2E





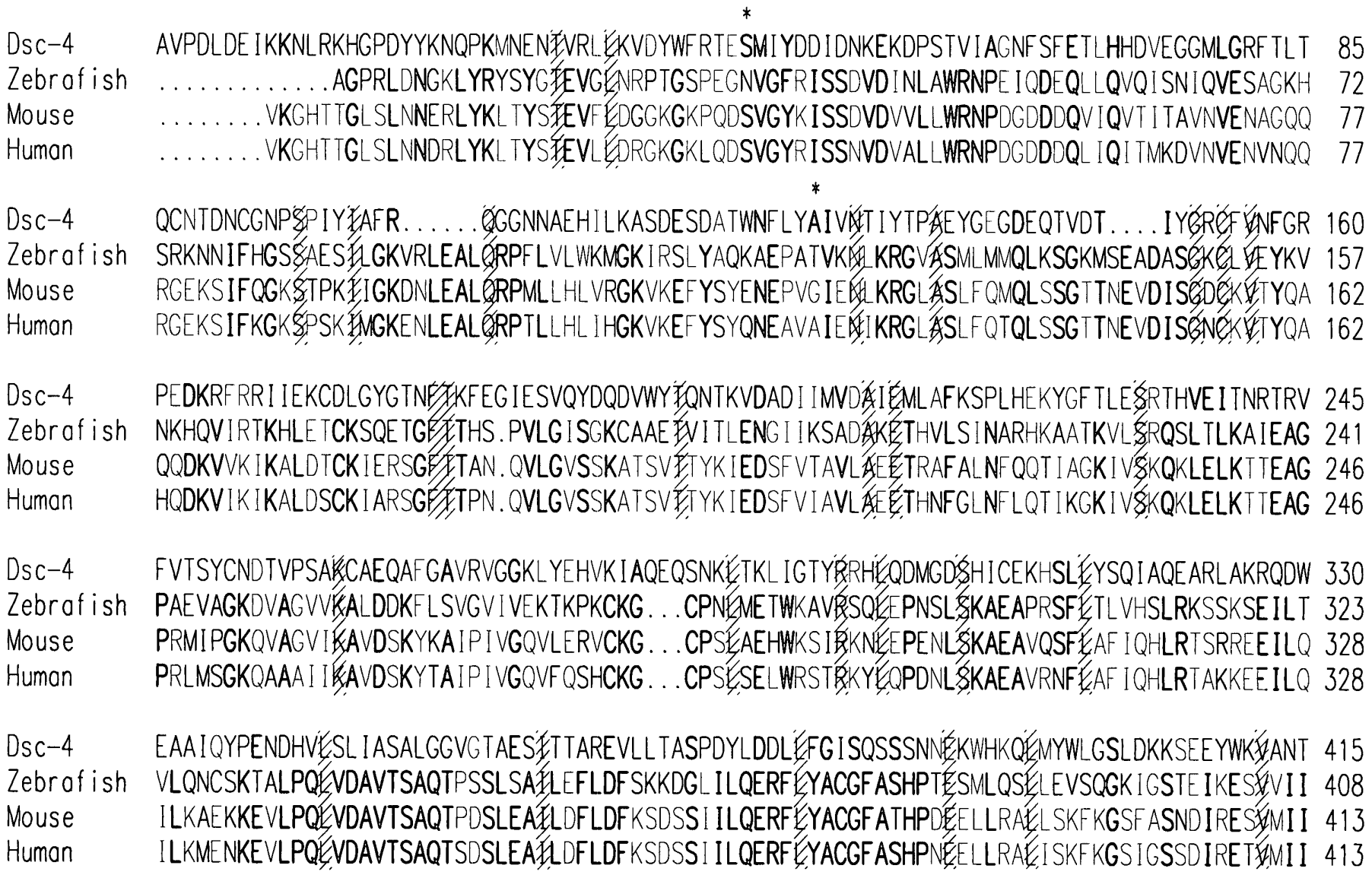

*
Dsc-4 AVPDLDEIKKNLRKHGPDYYKNQPKMNENTVRLLKVDYWFRTESMIYDDIDNKEKDPSTVIAGNFSFETLHHDVEGGMLGRFTLT 85
Zebrafish .....AGPRLDNGKLYRYSYGTEVGLNRPTGSPEGNVGFRISSDVDINLAWRNPEIQDEQLLQVQISNIQVESAGKH 72
Mouse .....VKGHTTGLSLNNERLYKLTYSTEVFLDGGKGKPQDSVGYKISSDVDVVLLWRNPDGDDDQVIQVTITAVNVENAGQQ 77
Human .....VKGHTTGLSLNNDRLYKLTYSTEVLLDRGKGKLQDSVGYRISSNVDVALLWRNPDGDDDQLIQITMKDVNVENVNQQ 77
*
Dsc-4 QCNTDNCGNPSPIYTAFR.....QGGNNAEHILKASDESDATWNFLYAIVNTIYTPAEYGEGDEQTVDT....IYGRCFVNFGR 160
Zebrafish SRKNNIFHGSSAESILGKVRLEALQRPFLVLWKMGKIRSLYAQKAEPATVKNLKRGVASMLMMQLKSGKMSEADASGKCLVEYKV 157
Mouse RGEKSIFQGKSTPKTIGKDNLEALQRPMLLHLVRGKVKEFYSYENEPVGIENLKRGLASLFQMQLSSGTTNEVDISGDCKVTYQA 162
Human RGEKSIFKGKSPSKTMGKENLEALQRPTLLHLIHGKVKEFYSYQNEAVAIENIKRGLASLFQTQLSSGTTNEVDISGNCKVTYQA 162
Dsc-4 PEDKRFRRIIEKCDLGYGTNFTKFEGIESVQYDQDVWYTQNTKVDADIIMVDAIEMLAFKSPLHEKYGFTLESRTHVEITNRTRV 245
Zebrafish NKHQVIRTKHLETCKSQETGFTTHS.PVLGISGKCAAETVITLENGIIKSADAKETHVLSINARHKAATKVLSRQSLTLKAIEAG 241
Mouse QQDKVVKIKALDTCKIERSGFTTAN.QVLGVSSKATSVTTYKIEDSFVTAVLAEETRAFALNFQQTIAGKIVSKQKLELKTTEAG 246
Human HQDKVIKIKALDSCKIARSGFTTPN.QVLGVSSKATSVTTYKIEDSFVIAVLAEETHNFGLNFLQTIKGKIVSKQKLELKTTEAG 246
Dsc-4 FVTSYCNDTVPSAKCAEQAFGAVRVGGKLYEHVKIAQEQSNKLTKLIGTYRRHLQDMGDSHICEKHSLEYSQIAQEARLAKRQDW 330
Zebrafish PAEVAGKDVAGVVKALDDKFLSVGVIVEKTKPKCKG...CPNLMETWKAVRSQLEPNSLSKAEAPRSFLTLVHSLRKSSKSEILT 323
Mouse PRMIPGKQVAGVIKAVDSKYKAIPIVGQVLERVCKG...CPSLAEHWKSIRKNLEPENLSKAEAVQSFLAFIQHLRTSRREEILQ 328
Human PRLMSGKQAAAIIKAVDSKYTAIPIVGQVFQSHCKG...CPSLSELWRSTRKYLQPDNLSKAEAVRNFLAFIQHLRTAKKEEILQ 328
Dsc-4 EAAIQYPENDHVLSLIASALGGVGTAESLTTARELVLLTASPDYLDDLLFGISQSSSNNEKWHKQLMYWLGSLDKKSEEYWKVANT 415
Zebrafish VLQNCSKTALPQLVDAVTSAQTPSSLSAILEFLDFSKKDGLILQERFLYACGFASHPTESMLQSLLEVSQGKIGSTEIKESVVII 408
Mouse ILKAEKKEVLPQLVDAVTSAQTPDSLEAILDFLDFKSDSSIILQERFLYACGFATHPDEELLRALLSKFKGSFASNDIRESVMII 413
Human ILKMENKEVLPQLVDAVTSAQTSDSLEAILDFLDFKSDSSIILQERFLYACGFASHPNEELLRALISKFKGSIGSSDIRETVMII 413

FIG.3A-1

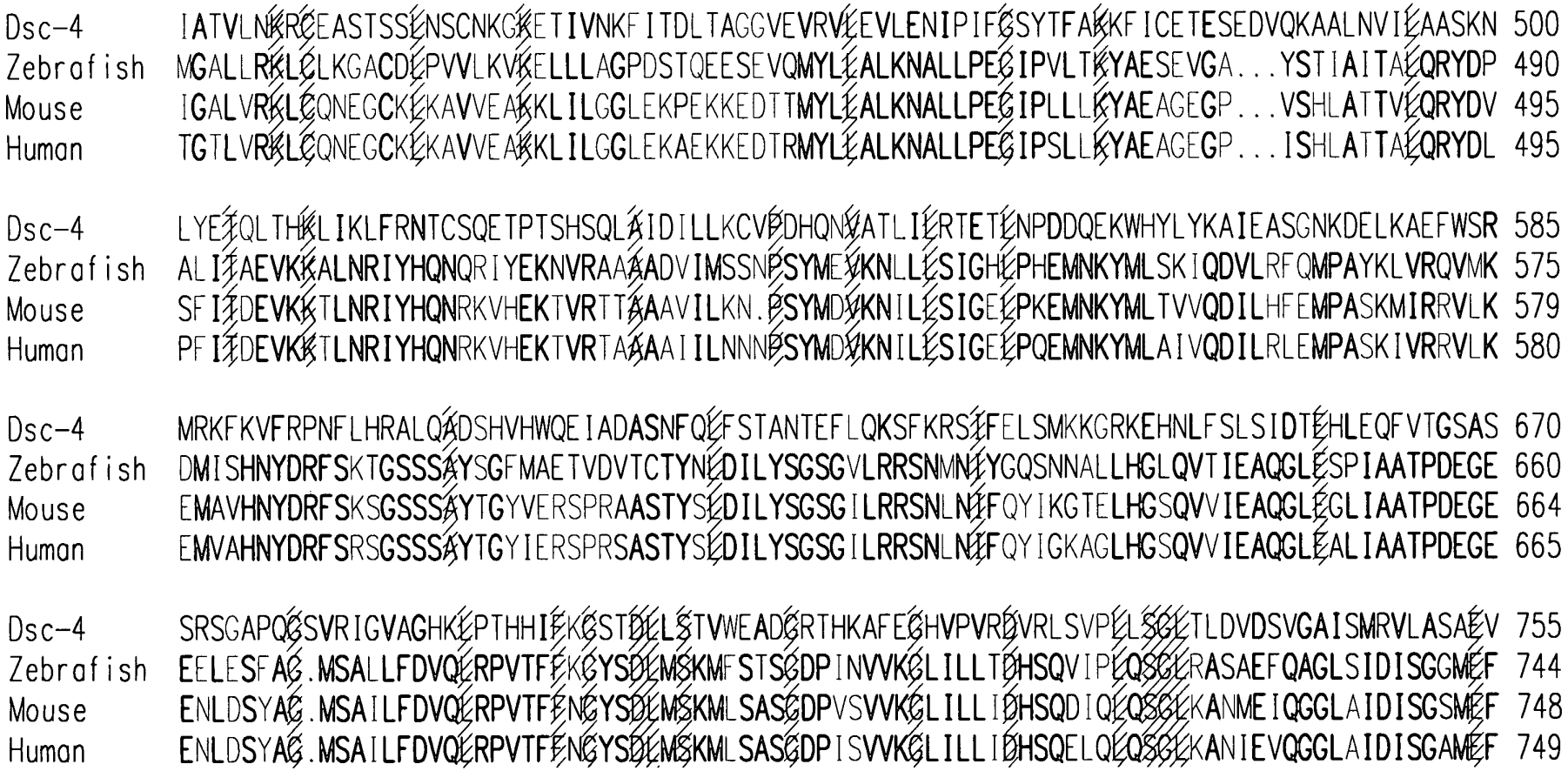

Dsc-4 IATVLNKRCEASTSSLNSCNKGKETIVNKFITDLTAGGVEVRVLEVLENIPIFGSYTFAKKFICETESEDVQKAALNVILAASKN 500
Zebrafish MGALLRKLCLKGACDLPVVLKVKELLLAGPDSTQEESEVQMYLLALKNALLPEGIPVLTKYAESEVGA...YSTIAITALQRYDP 490
Mouse IGALVRKLCQNEGCKLKAVVEAKKLILGGLEKPEKKEDTTMYLLALKNALLPEGIPLLLKYAEAGEGP...VSHLATTVLQRYDV 495
Human TGTLVRKLCQNEGCKLKAVVEAKKLILGGLEKAEKKEDTRMYLLALKNALLPEGIPSLLKYAEAGEGP...ISHLATTALQRYDL 495
Dsc-4 LYEIQLTHKLIKLFRNTCSQETPTSHSQLAIDILLKCVPDHQNVATLILRTETLNPDDQEKWHYLYKAIEASGNKDELKAEFWSR 585
Zebrafish ALIIAEVKKALNRIYHQNQRIYEKNVRAAAADVIMSSNPSYMEVKNLLLSIGHLPHEMNKYMLSKIQDVLRFQMPAYKLVRQVMK 575
Mouse SFIIDEVKKTLNRIYHQNRKVHEKTVRTTAAAVILKN.PSYMDVKNILLSIGELPKEMNKYMLTVVQDILHFEMPASKMIRRVLK 579
Human PFIIDEVKKTLNRIYHQNRKVHEKTVRTAAAAIILNNNPSYMDVKNILLSIGELPQEMNKYMLAIVQDILRLEMPASKIVRRVLK 580
Dsc-4 MRKFKVFRPNFLHRALQADSHVHWQEIADASNFQLFSTANTEFLQKSFKRSIFELSMKKGRKEHNLFSLSIDTEHLEQFVTGSAS 670
Zebrafish DMISHNYDRFSKTGSSSAYSGFMAETVDVTCTYNLDILYSGSGVLRRSNMNIYGQSNNALLHGLQVTIEAQGLESPIAATPDEGE 660
Mouse EMAVHNYDRFSKSGSSSAYTGYVERSPRAASTYSLDILYSGSGILRRSNLNIFQYIKGTELHGSQVVIEAQGLEGLIAATPDEGE 664
Human EMVAHNYDRFSRSGSSSAYTGYIERSPRSASTYSLDILYSGSGILRRSNLNIFQYIGKAGLHGSQVVIEAQGLEALIAATPDEGE 665
Dsc-4 SRSGAPQGSVRIGVAGHKLPTHHIFKGSTDLLSTVWEADGRTHKAFEGHVPVRDVRLSVPLLSGLTLDVDSVGAISMRVLASAEV 755
Zebrafish EELESFAG.MSALLFDVQLRPVTFFKGYSDLMSKMFSTSGDPINVVKGLILLTDHSQVIPLQSGLRASAEFQAGLSIDISGGMEF 744
Mouse ENLDSYAG.MSAILFDVQLRPVTFFNGYSDLMSKMLSASGDPVSVVKGLILLIDHSQDIQLQSGLKANMEIQGGLAIDISGSMEF 748
Human ENLDSYAG.MSAILFDVQLRPVTFFNGYSDLMSKMLSASGDPISVVKGLILLIDHSQELQLQSGLKANIEVQGGLAIDISGAMEF 749

FIG.3A-2

```
Dsc-4        SLWNQRS..NAKAEAYTSGSLHLTASLYHHSEPVRHVESTISALSTFTTDTRAIFETLPYDFCLRTSNSNVDINQKTVVQDQIGK 838
Zebrafish    SLWYRESKTSVNNRGALVIIGNMTVDTDFVSAGVEVGFETEATLDFITTVQFSEYPFLVCMQMDKTTFPFRETVSKQEKLPTGQM 829
Mouse        SLWYRESKTRVKNRVAVVITSDVTVDASFVKAGLESRAETEAGLEFISTVQFSQYPFLVCMQMDKAEAPLRQFETKYERLSTGRG 833
Human        SLWYRESKTRVKNRVTVVITTDITVDSSFVKAGLETSTETEAGLEFISTVQFSQYPFLVCMQMDKDEAPFRQFEKKYERLSTGRG 834

Dsc-4        HKKKTLNRKRVHPGVTYRLDDSTIRQCNSYLEQFRL..... 874
Zebrafish    FSRKRS.RDQVVPGSEFPLHQENSNMCKKVFEPAW..... 863
Mouse        YVSRRR.KESLVAGCELPLHQQNSEMCNVVFPPQPESDNSGGWF 876
Human        YVSQKR.KESVLAGCEFPLHQENSEMCKVVFAPQPDS.TSSGWF 876
```

FIG.3A-3

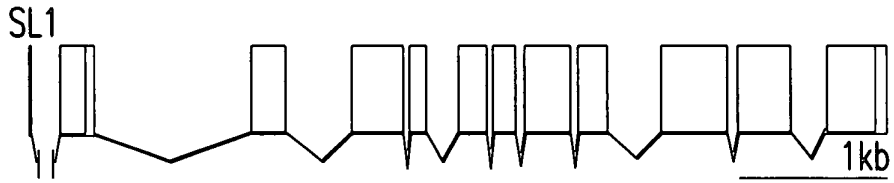


FIG.3B

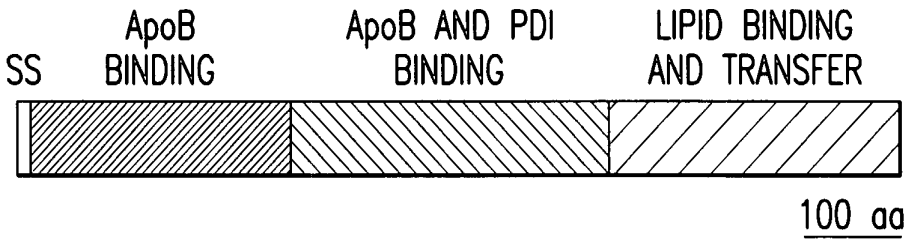


FIG.3C

```
1       TTTAATTACCCAAGTTTGAGTGTTATCAGCAAGCATAAAATCATAACTCTTATCAATAGTACTGCTTCTCTGCATCATTCACAATTCTTCTCTTCCATCCAAACA

106     GGACTCCATTGCCAATAAAATTATTTTAATTTTGCTCTCTCTGGGAGAAATTTGGAAACCAGAGATGTTCTCATCACGGATATGGCTGCTTCTGGCCGTTACTGT
1                                                                                 M  F  S  S  R  I  W  L  L  L  A  V  T  V

211     GGGAGTTTGCCTAGCAGTTCCGGATCTCGATGAAATCAAGAAGAACCTTCGCAAACATGGTCCAGACTACTATAAAAATCAGCCGAAAATGAACGAGAACACTGT
15        G  V  C  L  A  V  P  D  L  D  E  I  K  K  N  L  R  K  H  G  P  D  Y  Y  K  N  Q  P  K  M  N  E  N  T  V
                      ^                                    #
316     CCGACTACTGAAAGTGGATTACTGGTTCCGTACTGAATCTATGATTTACGATGATATTGATAATAAGGAGAAGGATCCATCGACCGTTATTGCTGGAAATTTCAG
50        R  L  L  K  V  D  Y  W  F  R  T  E  S  M  I  Y  D  D  I  D  N  K  E  K  D  P  S  T  V  I  A  G  N  F  S

421     CTTTGAAACACTTCATCATGACGTGGAGGGTGGCATGTTGGGACGGTTTACGCTAACCCAATGCAACACTGACAACTGTGGTAATCCATCTCCAATCTACATAGC
85        F  E  T  L  H  H  D  V  E  G  G  M  L  G  R  F  T  L  T  Q  C  N  T  D  N  C  G  N  P  S  P  I  Y  I  A
                  #
526     ATTCCGTCAAGGTGGTAATAATGCGGAGCATATCCTTAAAGCGTCCGATGAGAGTGACGCCACCTGGAATTTCCTGTACGCAATTGTGAATACAATCTACACGCC
120       F  R  Q  G  G  N  N  A  E  H  I  L  K  A  S  D  E  S  D  A  T  W  N  F  L  Y  A  I  V  N  T  I  Y  T  P

631     AGCAGAGTACGGAGAAGGAGACGAGCAAACAGTCGACACAATTTACGGAAGATGCTTCGTGAACTTTGGAAGGCCAGAGGATAAACGGTTTAGAAGAATTATCGA
155       A  E  Y  G  E  G  D  E  Q  T  V  D  T  I  Y  G  R  C  F  V  N  F  G  R  P  E  D  K  R  F  R  R  I  I  E

736     GAAGTGTGATTTGGGTTACGGCACAAATTTTACGAAATTCGAAGGAATCGAGAGTGTTCAATATGATCAGGATGTCTGGTACACACAGAACACAAAAGTCGATGC
190       K  C  D  L  G  Y  G  T  N  F  T  K  F  E  G  I  E  S  V  Q  Y  D  Q  D  V  W  Y  T  Q  N  T  K  V  D  A

841     AGACATTATTATGGTTGATGCTATTGAGATGTTAGCATTCAAGAGTCCACTTCACGAGAAATACGGATTCACTCTGGAATCCAGAACTCACGTAGAAATCACCAA
225       D  I  I  M  V  D  A  I  E  M  L  A  F  K  S  P  L  H  E  K  Y  G  F  T  L  E  S  R  T  H  V  E  I  T  N
```

FIG.4A

946 CCGTACACGTGTCTTCGTCACCAGCTACTGTAATGATACCGTACCATCCGCCAAATGCGCCGAGCAGGCGTTTGGAGCAGTTCGTGTCGGAGGAAAACTTTACGA
260 R T R V F V T S Y C N D T V P S A K C A E Q A F G A V R V G G K L Y E

1051 GCATGTCAAGATTGCGCAGGAACAGTCGAATAAGTTAACAAAGCTTATTGGAACATACCGCCGTCATCTTCAAGATATGGGTGACTCACACATTTGTGAGAAACA
295 H V K I A Q E Q S N K L T K L I G T Y R R H L Q D M G D S H I C E K H

1156 TTCTTTGCTTTATAGTCAAATTGCTCAAGAAGCCCGATTGGCTAAGCGACAGGACTGGGAAGCTGCTATCCAATACCCAGAGAATGATCATGTTCTATCTCTTAT
330 S L L Y S Q I A Q E A R L A K R Q D W E A A I Q Y P E N D H V L S L I

1261 CGCCAGTGCCCTCGGAGGAGTCGGTACAGCAGAATCTATCACCACTGCTCGTGAAGTTCTTCTTACCGCGTCCCCTGATTATCTTGATGATTTACTTTTTGGAAT
365 A S A L G G V G T A E S I T T A R E V L L T A S P D Y L D D L L F G I

1366 TTCACAAAGCTCGTCTAACAATGAGAAATGGCACAAACAATTGATGTACTGGCTCGGGTCCCTTGATAAAAAATCAGAAGAATATTGGAAGGTGGCTAACACAAT
400 S Q S S S N N E K W H K Q L M Y W L G S L D K K S E E Y W K V A N T I

1471 TGCAACTGTGCTGAACAAACGATGTGAAGCATCGACAAGCAGCTTAAACTCTTGCAATAAAGGAAAGGAAACGATTGTCAACAAATTCATCACTGACCTGACAGC
435 A T V L N K R C E A S T S S L N S C N K G K E T I V N K F I T D L T A

1576 TGGTGGAGTTGAAGTCAGAGTTCTCGAGGTTCTGGAGAATATTCCAATTTTCGGATCCTACACTTTTGCTAAGAAATTCATATGTGAAACTGAGTCGGAGGATGT
470 G G V E V R V L E V L E N I P I F G S Y T F A K K F I C E T E S E D V

1681 TCAGAAAGCCGCACTCAACGTTATTCTGGCTGCGAGCAAGAATTTGTATGAAACACAACTCACCCACAAGCTCATCAAACTCTTCCGCAACACATGCAGCCAGGA
505 Q K A A L N V I L A A S K N L Y E T Q L T H K L I K L F R N T C S Q E

1786 AACTCCAACTTCTCATTCTCAACTCGCCATCGACATTCTCCTCAAATGTGTCCCTGATCATCAAAACGTGGCCACCTTGATCCTGCGAACTGAGACTCTTAACCC
540 T P T S H S Q L A I D I L L K C V P D H Q N V A T L I L R T E T L N P

FIG.4B

```
1891  CGATGATCAGGAAAAATGGCATTACCTGTACAAGGCTATCGAGGCAAGCGGAAACAAGGATGAACTGAAGGCCGAATTTTGGTCGCGAATGCGGAAGTTTAAGGT
575    D  D  Q  E  K  W  H  Y  L  Y  K  A  I  E  A  S  G  N  K  D  E  L  K  A  E  F  W  S  R  M  R  K  F  K  V

1996  TTTCCGACCAAACTTCTTGCACAGAGCACTTCAGGCGGATTCTCATGTTCACTGGCAAGAGATTGCAGATGCTTCAAACTTCCAACTGTTCTCCACTGCGAACAC
610    F  R  P  N  F  L  H  R  A  L  Q  A  D  S  H  V  H  W  Q  E  I  A  D  A  S  N  F  Q  L  F  S  T  A  N  T

2101  AGAATTCTTGCAAAAATCCTTTAAGAGATCCATCTTTGAGCTATCGATGAAGAAGGGAAGGAAGGAGCACAATTTATTCTCGCTCTCCATCGACACTGAGCACCT
645    E  F  L  Q  K  S  F  K  R  S  I  F  E  L  S  M  K  K  G  R  K  E  H  N  L  F  S  L  S  I  D  T  E  H  L

2206  TGAGCAATTTGTGACTGGATCAGCTTCTTCAAGATCCGGCGCTCCACAAGGGTCTGTTCGAATTGGAGTTGCTGGTCACAAGCTACCAACTCACCACATCTTCAA
680    E  Q  F  V  T  G  S  A  S  S  R  S  G  A  P  Q  G  S  V  R  I  G  V  A  G  H  K  L  P  T  H  H  I  F  K

2311  GGGAAGTACTGACCTGCTTTCCACTGTCTGGGAAGCAGATGGAAGGACGCATAAGGCATTTGAAGGTCATGTTCCTGTTAGAGACGTTCGACTATCGGTGCCATT
715    G  S  T  D  L  L  S  T  V  W  E  A  D  G  R  T  H  K  A  F  E  G  H  V  P  V  R  D  V  R  L  S  V  P  L

2416  GCTCTCTGGATTGACTCTTGACGTTGATAGCGTTGGAGCAATTAGTATGAGAGTTCTTGCATCGGCGGAAGTTTCCCTTTGGAATCAGAGATCGAATGCAAAGGC
750    L  S  G  L  T  L  D  V  D  S  V  G  A  I  S  M  R  V  L  A  S  A  E  V  S  L  W  N  Q  R  S  N  A  K  A
```

FIG.4C

```
2521  AGAGGCATATACATCCGGATCCTTACACCTAACGGCTTCCCTCTACCATCACTCAGAACCAGTCCGCCACGTGGAATCCACAATCTCGGCGCTCTCCACCTTCAC
785     E  A  Y  T  S  G  S  L  H  L  T  A  S  L  Y  H  H  S  E  P  V  R  H  V  E  S  T  I  S  A  L  S  T  F  T

2626  CACAGACACCCGTGCAATTTTCGAGACTCTCCCATATGACTTCTGCCTAAGAACATCTAATAGCAATGTTGATATCAATCAGAAAACAGTTGTACAGGATCAAAT
820     T  D  T  R  A  I  F  E  T  L  P  Y  D  F  C  L  R  T  S  N  S  N  V  D  I  N  Q  K  T  V  V  Q  D  Q  I

2731  TGGAAAGCATAAAAAGAAGACGCTTAATCGAAAACGAGTACATCCTGGAGTTACATACAGGTTGGATGACTCGACGATTCGGCAGTGTAATAGTTATTTGGAGCA
855     G  K  H  K  K  K  T  L  N  R  K  R  V  H  P  G  V  T  Y  R  L  D  D  S  T  I  R  Q  C  N  S  Y  L  E  Q

2836  GTTTAGATTGTAGTTGTTTGTTTTTTTTATTAACATTTCATGTTTGTTCTGGAATCAAATAAAAAATAACTTATTGAGAAAAAAAAA
890     F  R  L  *
```

FIG.4D

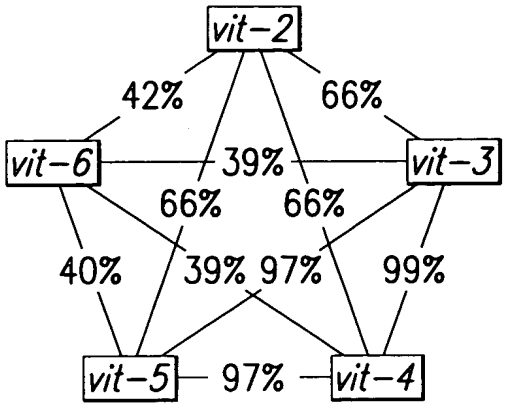

vit-2
42%
66%
vit-6
39%
vit-3
66%
66%
40%
39%
97%
99%
vit-5
97%
vit-4

FIG.5A

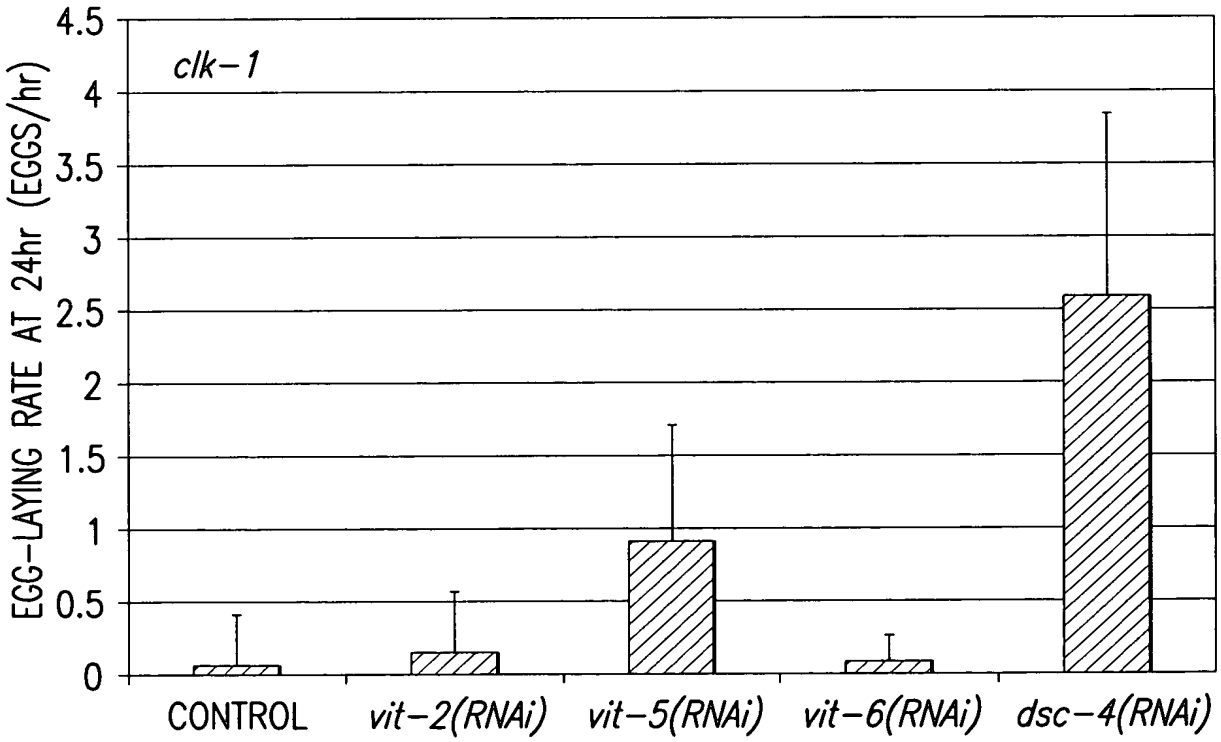

clk-1
EGG-LAYING RATE AT 24hr (EGGS/hr)
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
CONTROL
vit-2(RNAi)
vit-5(RNAi)
vit-6(RNAi)
dsc-4(RNAi)

FIG.5B

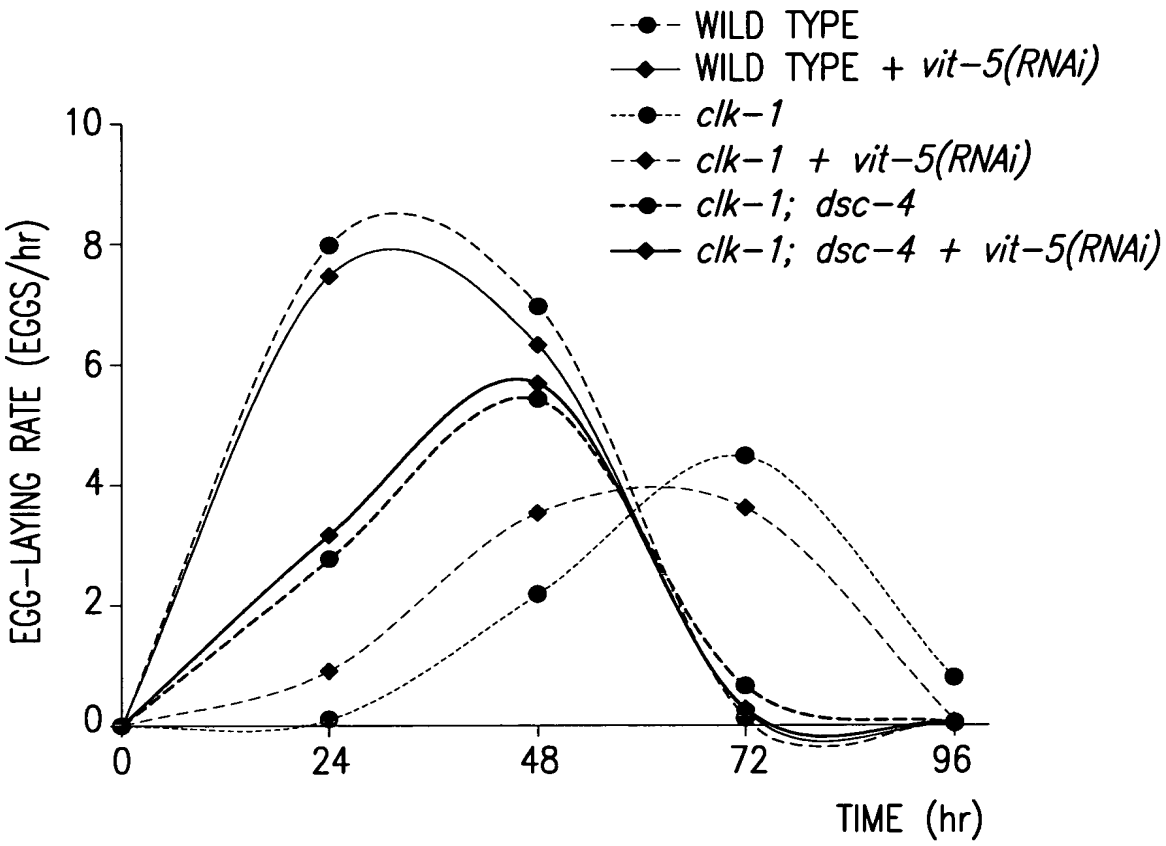

WILD TYPE
WILD TYPE + vit-5(RNAi)
clk-1
clk-1 + vit-5(RNAi)
clk-1; dsc-4
clk-1; dsc-4 + vit-5(RNAi)
EGG-LAYING RATE (EGGS/hr)
10
8
6
4
2
0
0
24
48
72
96
TIME (hr)

FIG.5C

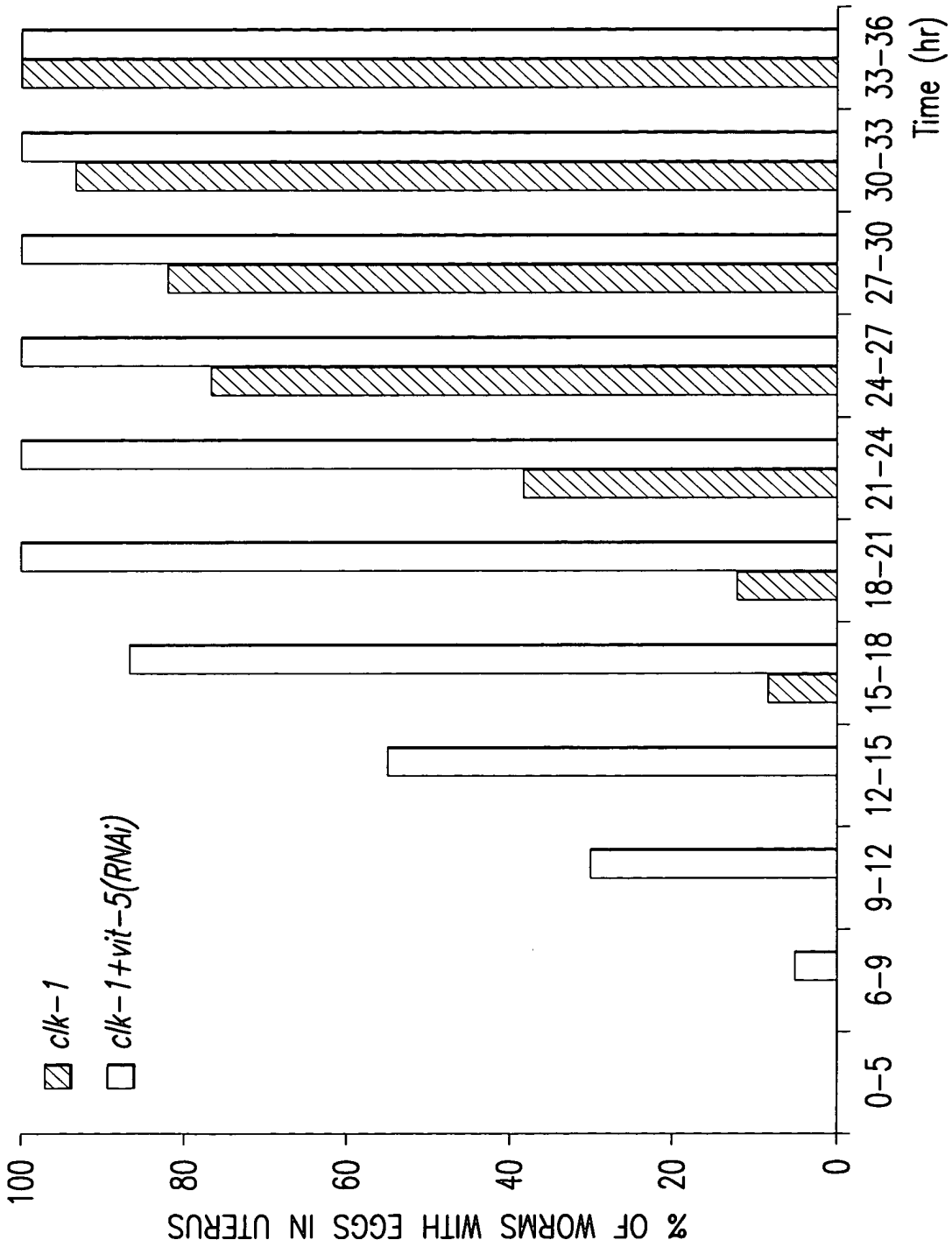

% OF WORMS WITH EGGS IN UTERUS
100
80
60
40
20
0
clk-1
clk-1+vit-5(RNAi)
0-5
6-9
9-12
12-15
15-18
18-21
21-24
24-27
27-30
30-33
33-36
Time (hr)

FIG. 5D

FIG.5E

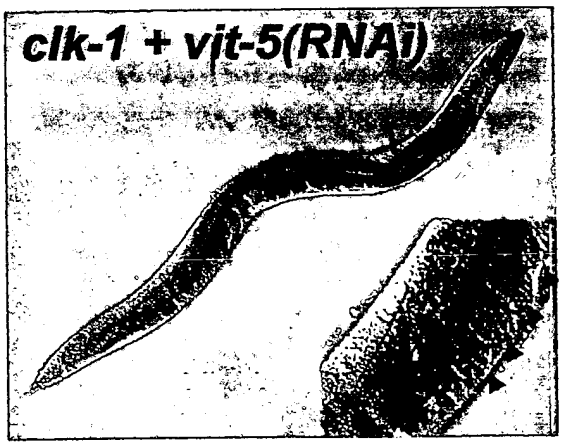


FIG.5F

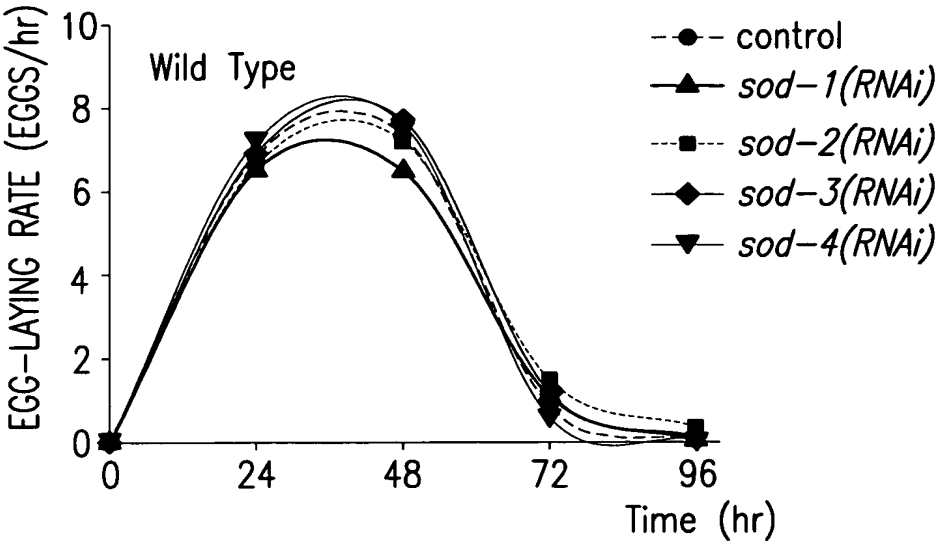

EGG-LAYING RATE (EGGS/hr)
10
8
6
4
2
0
Wild Type
0
24
48
72
96
Time (hr)
control
sod-1(RNAi)
sod-2(RNAi)
sod-3(RNAi)
sod-4(RNAi)

FIG.6A

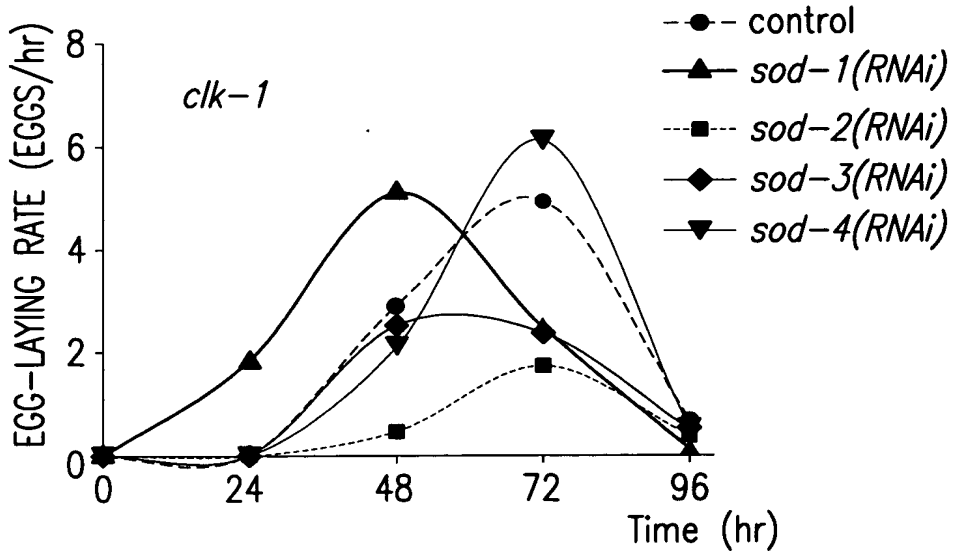

EGG-LAYING RATE (EGGS/hr)
8
6
4
2
0
clk-1
0
24
48
72
96
Time (hr)
control
sod-1(RNAi)
sod-2(RNAi)
sod-3(RNAi)
sod-4(RNAi)

FIG.6B

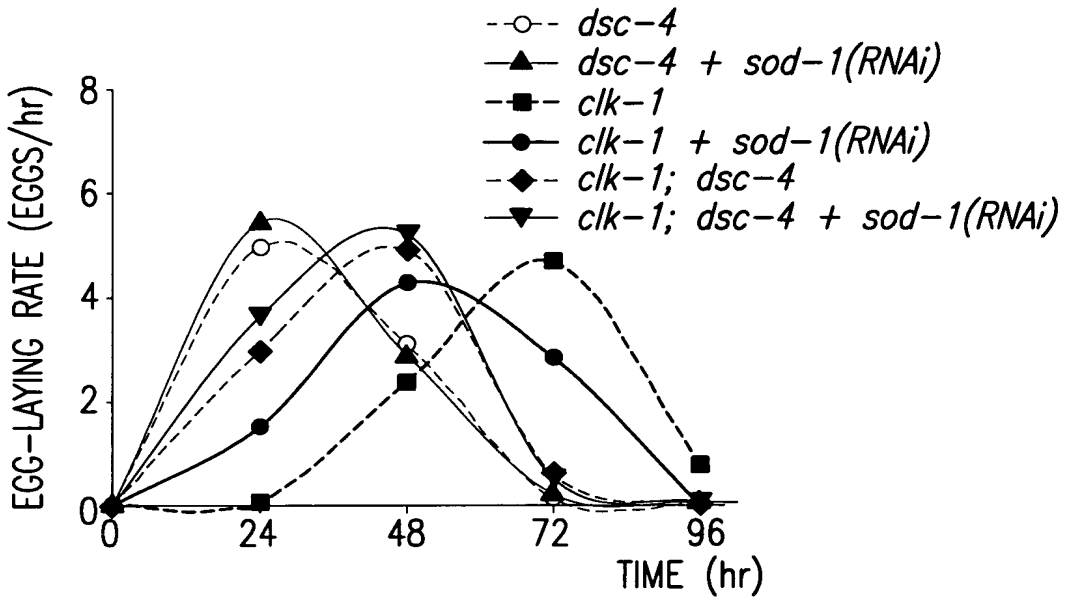

dsc-4
dsc-4 + sod-1(RNAi)
clk-1
clk-1 + sod-1(RNAi)
clk-1; dsc-4
clk-1; dsc-4 + sod-1(RNAi)
EGG-LAYING RATE (EGGS/hr)
0
2
4
6
8
0
24
48
72
96
TIME (hr)

FIG.6C

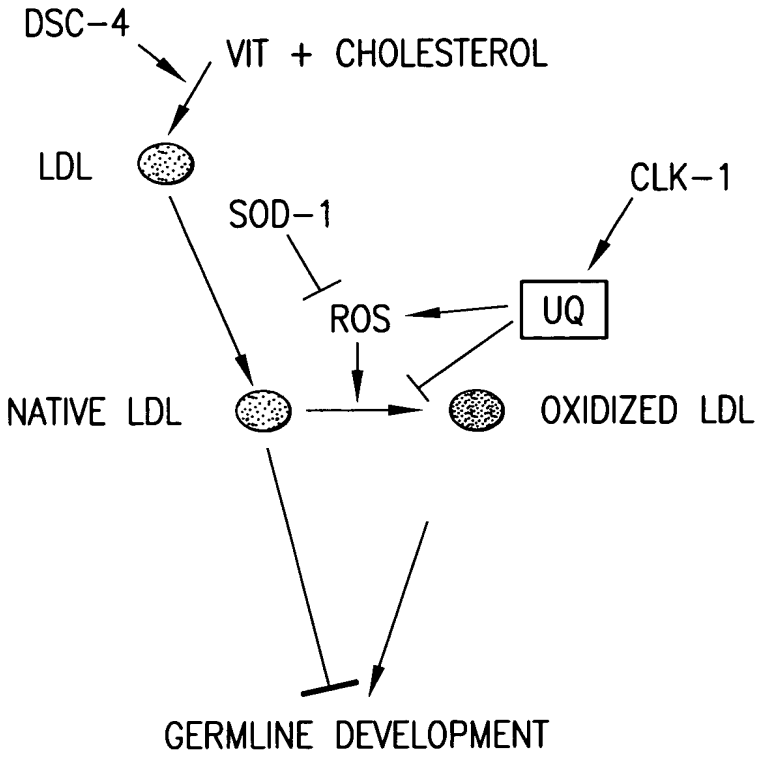

DSC-4
VIT + CHOLESTEROL
LDL
CLK-1
SOD-1
ROS
UQ
NATIVE LDL
OXIDIZED LDL
GERMLINE DEVELOPMENT

FIG.7A

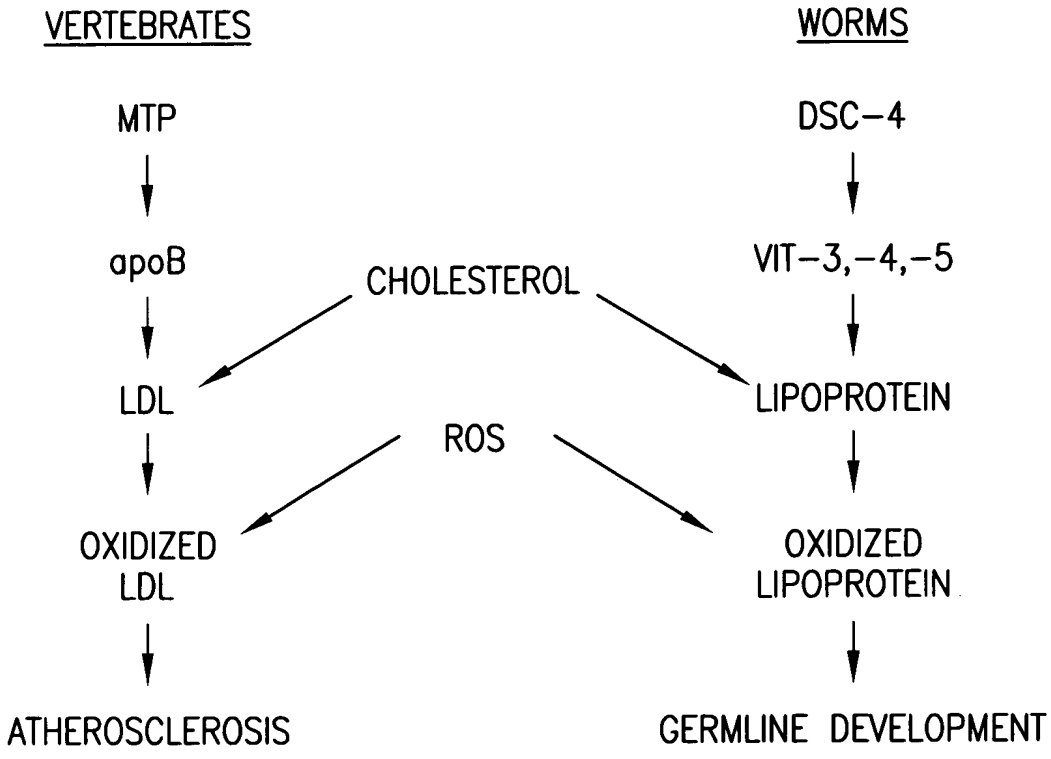

VERTEBRATES
WORMS
MTP
DSC-4
apoB
CHOLESTEROL
VIT-3,-4,-5
LDL
LIPOPROTEIN
ROS
OXIDIZED LDL
OXIDIZED LIPOPROTEIN
ATHEROSCLEROSIS
GERMLINE DEVELOPMENT

FIG.7B

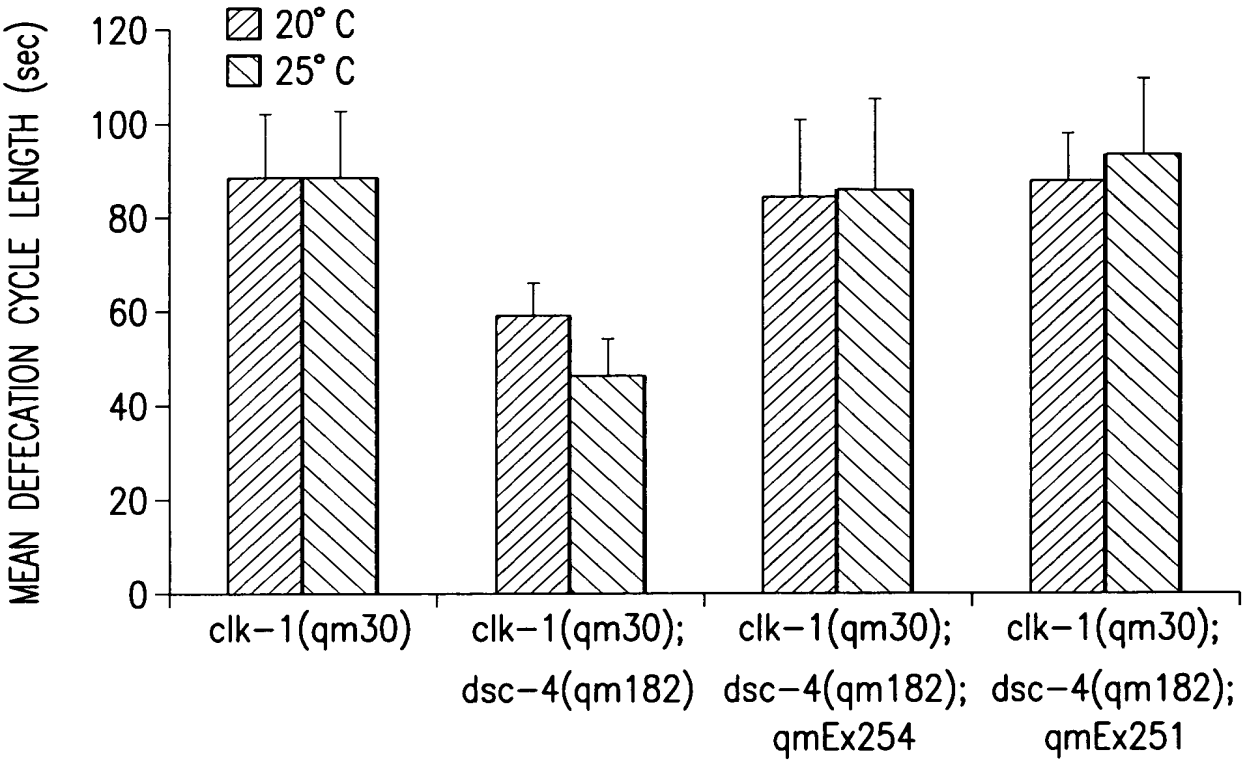

MEAN DEFECATION CYCLE LENGTH (sec)
120
100
80
60
40
20
0
20° C
25° C
clk-1(qm30)
clk-1(qm30); dsc-4(qm182)
clk-1(qm30); dsc-4(qm182); qmEx254
clk-1(qm30); dsc-4(qm182); qmEx251

FIG.8A

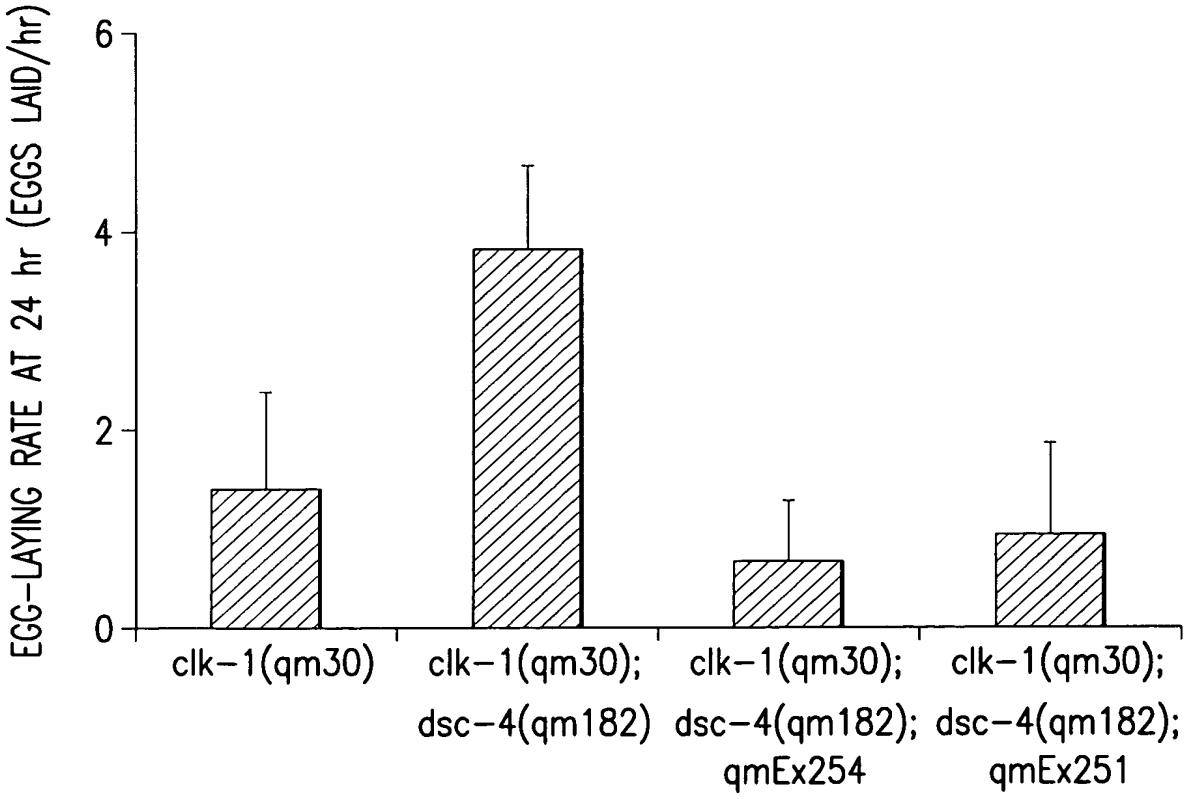

EGG-LAYING RATE AT 24 hr (EGGS LAID/hr)
6
4
2
0
clk-1(qm30)
clk-1(qm30); dsc-4(qm182)
clk-1(qm30); dsc-4(qm182); qmEx254
clk-1(qm30); dsc-4(qm182); qmEx251

FIG.8B

1 ATGTTCAGTT GGTTGCCATG CTGTTCAAGT ACTTCAAACG AAAAGAATGC GCCGACGGAA
61 CGAAGATTAC GAGCTAACGA TAGGGAATAT AATGCACAAT TCAAATATGC AGACAATGTA
121 ATCAAAACGT CCAAATACAA TATAATCACC TTCATTCCTC AAAATTTATT CGAACAATTC
181 CAGCGGATAG CCAACTTTTA TTTTTTAGTT TTAATGATAT TACAGTTTAT TCCTCAAATT
241 TCCTCAATTT CCTGGTATTC TACAGCGGTT CCACTGGTTA TTGTATTGGC ATTTTCAGCT
301 ATTAAAGATG GGTACGATGA TGCGCAAAGG CACATATCTG ATCGAAATGT AAATGGTCGA
361 AAATCCTACG TAGTTCGAAA TGGAAGTCTA TGTGAAGAAG ACTGGAGTAA TGTTAAAGTT
421 GGAGATGTGA TACGAATGAT GAGTAATCAA TTTGTGGCGG CTGATCTTCT ATTATTATCA
481 ACGTCGGAAC CATATGGAGT ATGTTTTATT GAAACTATGG AATTGGATGG AGAAACAAAT
541 CTGAAAAATC GTGCCGCTAT TGCATGTACC CAGGAAATGG GCGACGATTT GGATGGGATT
601 ACGCGCTTTG ATGGAGAAAT AATCTGTGAA CCTCCCAATA ACAAACTAGA CAAGTTCAAT
661 GGAAAATTAA TATGGAATAA TCATGAATAT GGAGTTAATA ATGATAATAT TCTGCTGAGA
721 GGATGTATTT TGAAGAACAC GAGATGGTGT TATGGAGTTG TCGTTTTTGC TGGAAAAGAT
781 ACAAAATTAA TGATGAACAG TGGAAAAACA AAGTTCAAAA GAACGTCTCT CGACCGATTT
841 TTGAATATTT TAATCGTCGG AATTGTGCTT TTTCTCATTG CAATGTGCCT AATTTGTACG
901 ATTTTGTGTG CTGTATGGGA ATATCAAACT GGAAGATATT TTACTATTTA TCTACCGTGG
961 GACGATGTGG TTCCTAGTCC TGAACAAAGA GGTGGCCGCC AAATTGCCCT TATCGCCTTC
1021 CTCCAGTTCT TCTCCTACAT CATTCTTCTC AATACAGTTG TACCAATTTC TTTATATGTG
1081 TCTGTGGAAA TTATTCGATT TATTCATTCA TTATGGATTA ATTACGACAC TCAAATGTAT
1141 TATGAAAATG GAGAGAAAAG TGTCCCAGCA AAGGCACATA CAACAACTTT AAATGAGGAG
1201 TTGGGACAAG TTCAATATGT GTTCAGTGAC AAGACTGGAA CGTTGACAAG GAATATTATG
1261 ACTTTTAATA AGTGTACCAT TAATGGGATC TCGTACGGAG ACATTTATGA TCACAAGGGA
1321 GAGGTTATTG AGACGAATGA CAAAACCAAA TCTCTCGACT TTTCCTGGAA TTCAGCGTCC
1381 GAACCCACAT TCAAATTTTT CGATAAAAAT CTAGTTGATG CTACAAAACG TCAAGTACCA
1441 GAAATTGATC AATTCTGGAG ACTACTGGCT CTTTGTCATA CTGTAATGCC TGAAAGAGAT
1501 AAAGGACAAC TGGTTTATCA GGCACAATCA CCTGATGAAC ATGCTCTAAC GTCAGCTGCA
1561 AGGAATTTTG GTTATGTTTT CCGAGCAAGA ACGCCTCAAA GCATTACGAT TGAAGTGATG
1621 GGAAATGAGG AAACTCATGA ATTATTGGCA ATTCTTGATT TTAATAATGA TCGAAAAAGA
1681 ATGTCTGTAA TTGTGAAAGG ACCTGATGGA AAGATTCGAT TGTATTGTAA AGGCGCTGAT
1741 ATGATGATTA TGCAGAGAAT ACATCCATCA ACATCTCAAA TAATGCGTAC CTCAACCAAT
1801 ACTCATCTCG CTGATTTTGC AAATATCGGT CTTCGAACGC TTTGTTTGGG ATACAAGGAT
1861 CTTGATCCAG CGTACTTTTC GGATTGGGAT TCTCGAGTCA AAAAGGCGTC CGCAGCCATG
1921 CAGGACAGAG AATCTGCGGT CGATGCTCTT TACGAAGAAA TTGAAAAAGA TCTGATATTG
1981 ATTGGTGCAA CGGCTATTGA AGACAAGCTT CAGGATGGTG TTCCAGAGGC AATTGCAAGA
2041 CTTTCAGAAG CTAATATCAA GATTTGGGTG CTTACCGGGG ATAAGACAGA AACGGCTATA
2101 AACATTGCCT ACTCGTGTCG CCTTCTGACC GATGAAACCA AGGAAATTGT TGTAGTTGAT
2161 GGGCAAACTG ATACCGAAGT CGAAGTACAG CTAAAAGATA CAAGAAACAC ATTTGAACAG
2221 ATTTTGGCAT TGCCGTCACC GCTTGGAGGA AAGCCACGTA TTGAAATTGA GACAATCCAC
2281 GAGGAGTCCG AGGCTATTTC CTCTGCAAGG AGTATGGATA GAAACATTGT AACTCCTGAT
2341 TTGAAATCAG CAGAAATGGC TGAACACGAG AGTGGAGGTG TTGCTTTGGT AATAAATGGA

FIG.9A

2401 GATTCATTGG CTTTTGCTCT TGGTCCAAGA CTTGAAAGAA CTTTTCTTGA AGTGGCTTGT
2461 ATGTGTAATG CAGTAATATG TTGCCGAGTG ACACCACTTC AAAAAGCTCA AGTAGTTGAT
2521 CTAGTAAAAC GAAACAAAAA AGCAGTGACA CTTTCAATTG GAGACGGAGC AAATGATGTC
2581 AGTATGATCA AGACAGCTCA TATTGGAGTT GGAATTTCTG GCCAAGAAGG AATGCAAGCA
2641 GTATTAGCAT CAGACTATTC AATCGGACAA TTCAAATATC TTGAACGTCT TCTTCTTGTT
2701 CACGGTCGAT GGTCTTACAT TCGAATGGCA AAGTTCCTCA GATACTTTTT TTACAAAAAC
2761 TTTGCATTTA CACTTACCAA CTTCTGGTAT TCATTCTTCT GTGGATATTC TGCTCAAACA
2821 GTTTTTGACG CTGTATTGAT TGCTTGTTAC AATCTCTTTT TCACAGCACT TCCTGTTTTG
2881 GCAATGGGAT CTTTGGATCA AGATGTTGAT GATCATTATT CACTGAGATA TCCTAAGCTT
2941 TATCTGCCGG GACAGTTCAA TTTGTTCTTT AATATGAGAA TATTTATTTA TTCTGTACTT
3001 CATGGAATGT TTAGTTCCCT TGTGATATTC TTCATTCCAT ATGGTGCATT TTACAACGCA
3061 GCTGCTGCTT CTGGAAAGGA TTTGGACGAT TACTCGGCTC TTGCTTTCAC TACTTTTACT
3121 GCATTAGTTG TAGTTGTTAC TGGACAGATA GCCTTCGACA CGAGTTATTG GACGGCAATT
3181 TCGCATTTTG TAATCTGGGG ATCACTTGTT CTGTATTTCC TTGTTTGCTT CCTTCTTTAC
3241 GAATGGCTTC CAGTTTCATG GATTGTCAAA ACATCATCTT CAATCTCATA TGGTGTCGCT
3301 TTTCGAACAA TGGTTACTCC TCACTTCTGG TTTTCAATTC TAATGGTTTC AGTTGTACTG
3361 TTACTACCAG TTATGCTTAA TCGATTCTTC TGGCTTGATA CACATCCATC ATTTGCTGAT
3421 AGGCTGAGAA TTCGAAAGAA AATGGGCAAG AAACCATCGG CGAAAGATGA TAAAAAAACC
3481 GCATTCAAAC GCACGGCAGC AACTCGACGA AGTGTCCGTG GATCACTTAG AAGTGGTTAC
3541 GCATTCTCTC ATTCACAAGG ATTCGGAGAA CTCATTCTCA AAGGAAAATT GTTCAAAAAT
3601 GTGGAAAATC TACGGGGAAA GAATAATTCG AATGCGAAAA TTCACCCGAC TTCTGATGAC
3661 TTGCAGCCGA TGCTTATTTC TAGTGTGCCT GATGACAGCC AAGGAGCTTC AAGTATTAAT
3721 GCAATGCACC TTCCAATGGG TACACGTCCA CAGAATGTAC CCCATACATT GAATGTAAAT
3781 ACTGATGACT GGTCTCAATC ATCGGATTTC CGTCCAGCCT ATGCAAAGGA ACCATCACCA
3841 CTGCAGGGTA CAGTAATCCG TGGCGATGGA CGGAGCCATA GAAACCACGT GTATTCGCGG
3901 GAAACTCAGG TCGAAGAACA ACCAGACGTA ATCACTCGCC TTTAA

FIG.9B

```
1       MFSWLPCCSS TSNEKNAPTE RRLRANDREY NAQFKYADNV IKTSKYNIIT FIPQNLFEQF
61      QRIANFYFLV LMILQFIPQI SSISWYSTAV PLVIVLAFSA IKDGYDDAQR HISDRNVNGR
121     KSYVVRNGSL CEEDWSNVKV GDVIRMMSNQ FVAADLLLLS TSEPYGVCFI ETMELDGETN
181     LKNRAAIACT QEMGDDLDGI TRFDGEIICE PPNNKLDKFN GKLIWNNHEY GVNNDNILLR
241     GCILKNTRWC YGVVVFAGKD TKLMMNSGKT KFKRTSLDRF LNILIVGIVL FLIAMCLICT
301     ILCAVWEYQT GRYFTIYLPW DDVVPSPEQR GGRQIALIAF LQFFSYIILL NTVVPISLYV
361     SVEIIRFIHS LWINYDTQMY YENGEKSVPA KAHTTTLNEE LGQVQYVFSD KTGTLTRNIM
421     TFNKCTINGI SYGDIYDHKG EVIETNDKTK SLDFSWNSAS EPTFKFFDKN LVDATKRQVP
481     EIDQFWRLLA LCHTVMPERD KGQLVYQAQS PDEHALTSAA RNFGYVFRAR TPQSITIEVM
541     GNEETHELLA ILDFNNDRKR MSVIVKGPDG KIRLYCKGAD MMIMQRIHPS TSQIMRTSTN
601     THLADFANIG LRTLCLGYKD LDPAYFSDWD SRVKKASAAM QDRESAVDAL YEEIEKDLIL
661     IGATAIEDKL QDGVPEAIAR LSEANIKIWV LTGDKTETAI NIAYSCRLLT DETKEIVVVD
721     GQTDTEVEVQ LKDTRNTFEQ ILALPSPLGG KPRIEIETIH EESEAISSAR SMDRNIVTPD
781     LKSAEMAEHE SGGVALVING DSLAFALGPR LERTFLEVAC MCNAVICCRV TPLQKAQVVD
841     LVKRNKKAVT LSIGDGANDV SMIKTAHIGV GISGQEGMQA VLASDYSIGQ FKYLERLLLV
901     HGRWSYIRMA KFLRYFFYKN FAFTLTNFWY SFFCGYSAQT VFDAVLIACY NLFFTALPVL
961     AMGSLDQDVD DHYSLRYPKL YLPGQFNLFF NMRIFIYSVL HGMFSSLVIF FIPYGAFYNA
1021    AAASGKDLDD YSALAFTTFT ALVVVVTGQI AFDTSYWTAI SHFVIWGSLV LYFLVCFLLY
1081    EWLPVSWIVK TSSSISYGVA FRTMVTPHFW FSILMVSVVL LLPVMLNRFF WLDTHPSFAD
1141    RLRIRKKMGK KPSAKDDKKT AFKRTAATRR SVRGSLRSGY AFSHSQGFGE LILKGKLFKN
1201    VENLRGKNNS NAKIHPTSDD LQPMLISSVP DDSQGASSIN AMHLPMGTRP QNVPHTLNVN
1261    TDDWSQSSDF RPAYAKEPSP LQGTVIRGDG RSHRNHVYSR ETQVEEQPDV ITRL*
```

FIG. 10

```
H06H21.10a  ..........................................................  0
ATP8B1      ..........................................................  0
ATP8B2      ..........................................................  0
ATP8B3      MGHHPAASSASRTVGGVPSPVWSWALCTELASLSALPRDRDCTQMDRWHRANGSTTSAALDARGLPPPASPAPTP  75
ATP8B4      ..........................................................  0
Consensus

H06H21.10a  ..........................................................  0
ATP8B1      ..........................................................  0
ATP8B2      ..........................................................  0
ATP8B3      RSTRAGPEPSPAPPGPGDTGDSDVTQEGSGPAGIRGVEKIPGSSDDVRLPPSPPSEFAAQPGGVSGCPRQDTQPM  150
ATP8B4      ..........................................................  0
Consensus

H06H21.10a  ..........................................................MFSWLPCCSSTSNEKNAPT  19
ATP8B1      MSTERDSETTFDEDSQPNDEVVPYSDDETEDELDDQGSAVEPEQNRVNREAEENREPFRKECTWQVKANDRKYHE  75
ATP8B2      ..............................MDTLRAVPLFSISGLFSFPYRVSHGIAGILLGEMAVCAKKRPPEE  45
ATP8B3      AGHSEPGGEAADDECGSPTSMGSLGQREDLQDEDRNSAF..........................TWKVQANNRAYNG  199
ATP8B4      ..........................................................  0
Consensus

H06H21.10a  ERRLRANDREYNAQFKYADNVIKTSKYNIITFIPQNLFEQFQRIANFYFLVLMILQFIPQISSISWYSTAVPLVI  94
ATP8B1      QPHFMNTKFLCIKESKYANNAIKTYKYNAFTFIPMNLFEQFKRAANLYFLALLILQAVPQISTLAWYTTLVPLLV  75
ATP8B2      ERRARANDREYNEKFQYASNCIKTSKYNILTFLPVNLFEQFQEVANTYFLFLLILQLIPQISSLSWFTTIVPLVL  120
ATP8B3      QFKEKVI..LCWQRKKYKTNVIRTAKYNFYSFLPLNLYEQFHRVSNLFFLIIIILQSIPDISTLPWFSLSTPMVC  274
ATP8B4      ..........................................................  0
Consensus
```

FIG. 11A

Docket No.: 302087-999008
Serial No.: TBA
Inventor(s): Hekimi et al.
Title: Screening Assays for Targets and Drugs Useful in Treatment and Prevention of Lipid Metabolic Disorders.

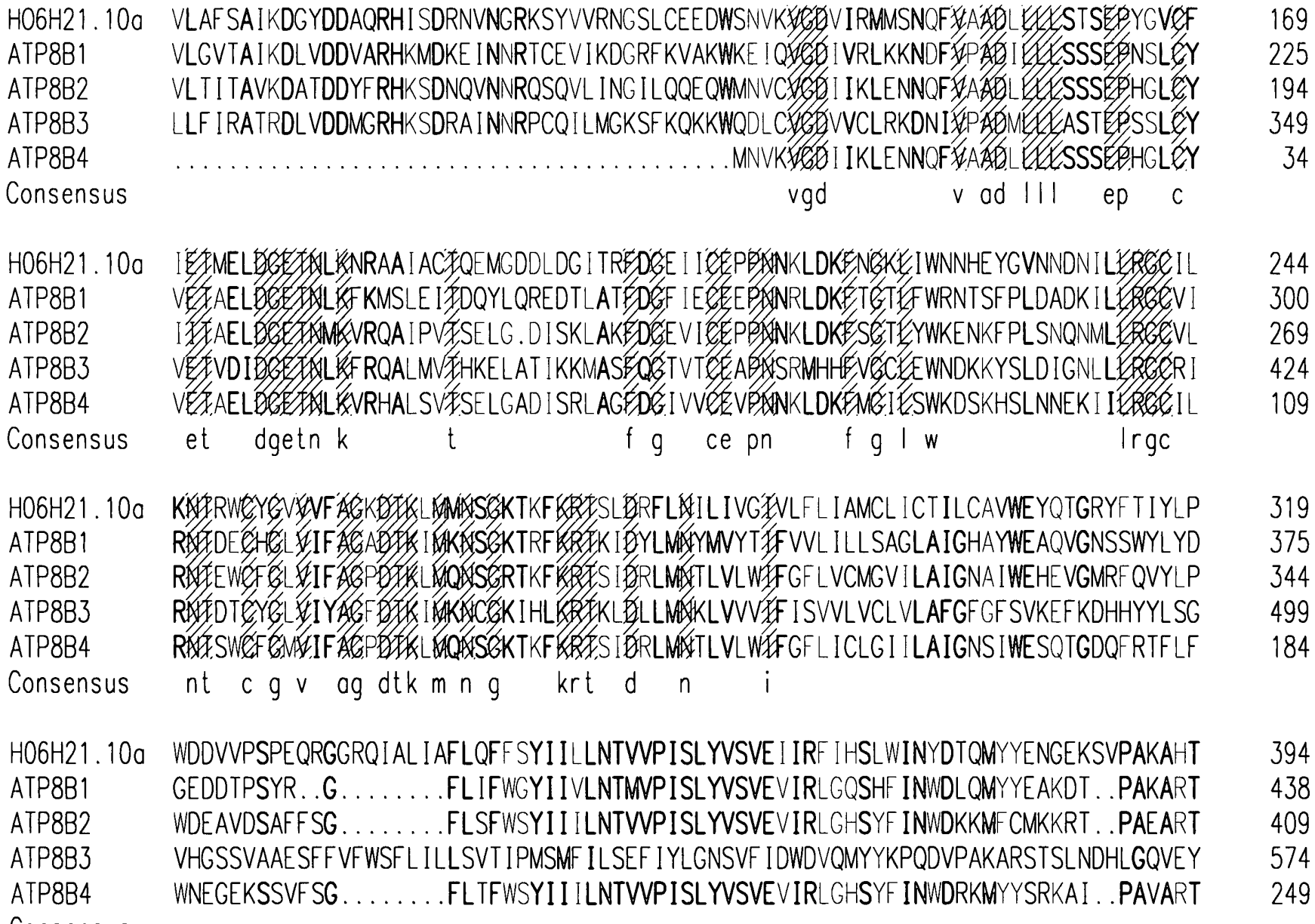


FIG. 11B

Docket No.: 302087-999008
Serial No.: TBA
Inventor(s): Hekimi et al.
Title: Screening Assays for Targets and Drugs Useful in Treatment and Prevention of Lipid Metabolic Disorders.

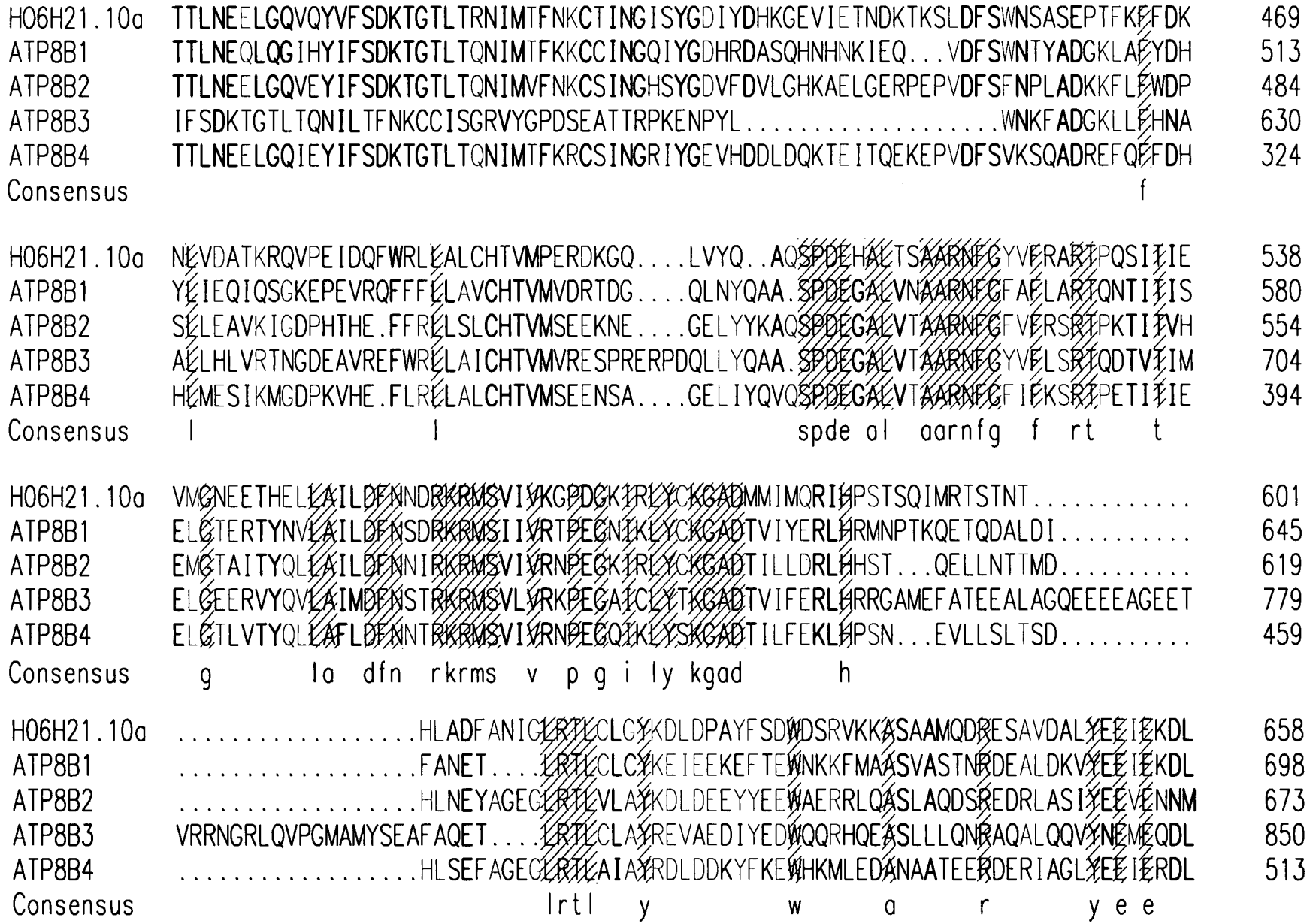


FIG.11C

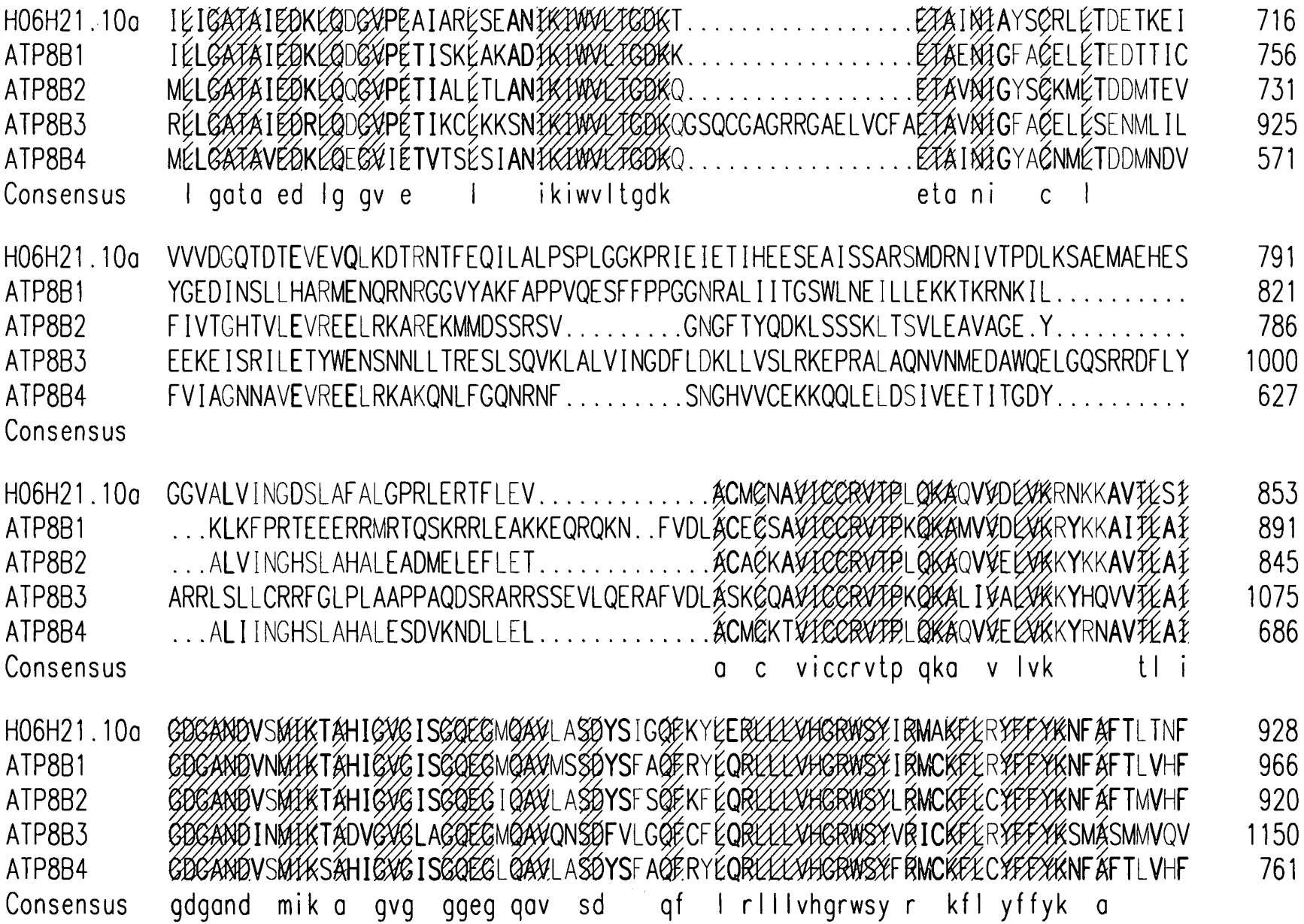


FIG.11D

FIG.11E

```
H06H21.10a  MLISSVPDDSQGASSINAMHLPMGTRPQNVPHTLNVNTDDWSQSSDFRPAYAKEPSPLQGTVIRGDGRSHRNHVY  1298
ATP8B1      LDAIVADGTAEYRRTGDS.....                                                      1251
ATP8B2      ASSPSGGADKPLKG.....                                                          1223
ATP8B3      EEKVEEGPSEEIFTMEPLPHVHRESRARRSSYAFSHREGYANLITQGTILRRGPGVSSDIASESLDPSDEEAASS  1490
ATP8B4      VSSFSQDKTVKL.....                                                            1065
Consensus

H06H21.10a  SRETQVEEQPDVITRL                                                             1314
ATP8B1      ................                                                             1251
ATP8B2      ................                                                             1223
ATP8B3      PKESQ...........                                                             1495
ATP8B4      ................                                                             1065
Consensus
```

FIG.11F